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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/600,648	10/17/2000	Shalaby Wahba Shalaby	00537-165002	9033

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EXAMINER	
NAFF, DAVID M	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 09/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/600,648	SHALABY, SHALABY WAHBA	
	Examiner	Art Unit	
	David M. Naff	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/28/05 has been entered.

An amendment submitted 6/28/05 amended claim 1.

Claims examined on the merits are 1-48, which are all claims in the application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 1-48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 has been amended to require the core to be substantially free of the peptide, protein or combination thereof. However, the claim language of the core being substantially free of the peptide, protein or combination thereof is not found in the specification, and support for the amendment to claim 1 is not found in the

specification. If the specification recites the claimed language added by the amendment, the pages and lines where the language is recited should be pointed out.

Claim Rejections - 35 USC § 112

Claims 1-48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are unclear as to the difference in the subsurface and the core of the microparticle. It is unclear as to the part of the microparticle that is the subsurface and the part that is the core. Both the subsurface and core are below the surface, and it is uncertain as to the distance from the surface, the subsurface changes to a core. It is suggested the subsurface be defined as crevices on the surface as set forth in the specification at page 14, lines 6-7.

Claim Rejections - 35 USC § 103

Claims 1-11, 22, 23, 26-33 and 47 rejected under 35 U.S.C. 103(a) as being unpatentable over Shalaby et al (5,672,659) or Ignatious et al (WO 97/39738) in view of Shalaby (5,612,052) and Chesterfield et al (5,366,756).

The claims are drawn to a bound microparticle comprising an absorbable heterochain polymer core and one or more peptides and/or proteins ionically immobilized on the surface and immediate subsurface of a core. The core is substantially free of the peptide, protein or combination thereof.

Shalaby et al ('659) and Ignatious et al disclose a composition containing a carboxyl group-containing polymer that can be a heterochain polymer ionically conjugated (col 2, line 65 of Shalaby et al and page 1, line 23 of Ignatious et al) with a bioactive polypeptide or a drug that is a polypeptide. The conjugate may be formed into microparticles. The conjugate is formed by combining a solution of the polymer with a solution of the polypeptide. See cols 2 and 3 of Shalaby et al and pages 4-9 of Ignatious et al.

Shalaby et al ('052) discloses coating microparticles with a drug to provide controlled release of the drug (col 7, lines 30-33).

Chesterfield et al disclose polymer particles coated with a tissue growth promoter and if desired a therapeutic agent for implanting to repair tissue (cols 1-3).

The present invention differ from Shalaby et al ('659) and Ignatious et al in that in the claims the polymer is formed into a microparticle and the polypeptide or protein is immobilized on the microparticle, whereas Shalaby et al and Ignatious et al form the conjugate by combining solutions of the polymer and polypeptide or protein and form a microparticle of the conjugate.

It would have been obvious to form the polymer of Shalaby et al ('659) or Ignatious et al into a microparticle prior to conjugating with the polypeptide or protein as suggested by Shalaby et al ('052) and Chesterfield et al forming a polymer microparticle and immobilizing a drug and/or growth promoter on the microparticle. Forming the microparticle before binding the protein or polypeptide

would have been expected to provide the protein or polypeptide on the surface of the microparticle and make it more readily available. When coating the microparticle as suggested by Shalaby ('052) and Chesterfield et al, the polypeptide will inherently be on the surface and subsurface of the microparticle, and the interior of the microparticle inherently be substantially free of the polypeptide. The conditions of dependent claims would have been matters of obvious choice in view of conditions disclosed by the references.

Response to Arguments

Applicant urges that to establish a *prima facie* case of obviousness, there must be motivation, a reasonable expectation of success and the prior art must teach or suggest all claim limitations. The argument is unpersuasive since it is believed these three criteria for *prima facie* obviousness have been met. Motivation would have been to provide the peptide or protein on the surface of the microparticle to be more readily available for release. Obviously, the peptide or protein will be more difficult to release if entrapped in the interior of the microparticle. If it had not been beneficial to provide the peptide or protein on the microparticle surface, Shalaby et al ('052) would not have coated the microparticle with the drug, but would have provided the drug within the microparticle as disclosed by Shalaby et al ('659) and Ignatious et al by mixing the drug with a solution of the polymer and forming microparticles. There is clearly a releasable expectation of success since Shalaby et al ('052) successfully coat microparticles with a drug to provide controlled release, and

Chesterfield et al successfully coat a tissue growth promoter on microparticles for implanting where the growth promoter functions *in vivo*. There is seen no reason why the polypeptide of Shalaby et al ('052) and Ignatious et al cannot be coated on an already formed microparticle. The references in combination suggest all limitations of the claims. If the polypeptide is coated on surface of the microparticle, the interior of the microparticle will inherently be substantially free of the polypeptide.

Claim Rejections - 35 USC § 103

Claims 12-21, 24, 25, 34-46 and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over the references as applied to claims 1-11, 22, 23, 26-33 and 47 above, and further in view of Auer et al (WO 92/11844) and Demian et al (5,795,922).

The claims require the bound microparticle containing the immobilized protein or polypeptide to be encased.

Auer et al disclose forming a complex of a protein pharmaceutical agent and a polycationic reagent, and encapsulating the complex in a microsphere (pages 4-9) to provide sustained release of the protein.

Demian et al disclose microencapsulating radiopacifier particles to prevent agglomerating (col 3).

When modifying Shalaby et al ('659) or Ignatious et al by forming the polymer into a microparticle before binding the protein or polypeptide as set form above, it would have been obvious to encapsulate the protein or polypeptide-containing microparticle as

suggested Auer et al to provide sustained release and as suggested by Demian et al to prevent agglomerating.

Response to Arguments

Applicant urges that the references applied in this rejection do not render the base claim obvious. However, the base claim is rendered obvious for reasons set forth above, and the present references are relied on to show the obviousness of the presently rejected claims.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David M. Naff whose telephone number is 571-272-0920. The examiner can normally be reached on Monday-Friday 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 751-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David M. Naff
Primary Examiner
Art Unit 1651

DMN
9/17/05